

IN THE CLAIMS

1. (original): A method of separating a target oligonucleotide from an impurity, in a mixture comprising said target oligonucleotide and said impurity, using a titratable anion exchange composition, comprising the steps:
 - a) binding said target oligonucleotide to said titratable anion exchange composition;
 - b) passing a solution through said titratable anion exchange composition with target oligonucleotide bound thereon, wherein said solution increases in pH over time; and
 - c) eluting said target oligonucleotide, wherein said impurity elutes at a different pH than said target oligonucleotide.
2. (original): The method of claim 1 wherein said titratable anion exchange composition comprises a primary amine, a secondary amine or a tertiary amine.
3. (original): The method of claim 1 or claim 2, wherein said titratable anion exchange composition comprises polyethyleneimine, polyimidazole, polyhistidine or polylysine.
4. (currently amended): The method of ~~any preceding~~ claim 1, wherein said solution in b) is substantially free of metal salts.
5. (currently amended): The method according to ~~any preceding~~ claim 1, wherein the solution in b) does not substantially increase its salt concentration over time.
6. (currently amended): The method of ~~any preceding~~ claim 1, wherein said titratable anion exchange composition is conjugated to a support.
7. (original): The method of claim 6, wherein said support is a synthetic polymer.
8. (original): The method of claim 7, wherein said synthetic polymer is selected from the group consisting of silica gel, a polysaccharide, a styrene-divinyl benzene copolymer, a polyethylene, a polypropylene, a polyacrylic and an agarose.

9. (currently amended): The method of claim 8, wherein said titratable anion exchange composition is polyethyleneimine-derivatized silica gel or a polyethyleneimine-derivatized derivatized styrene-divinyl benzene copolymer.
10. (currently amended): The method of ~~any preceding~~ claim 1, wherein said target oligonucleotide is a synthetic oligonucleotide.
11. (currently amended): The method of ~~Claim~~ claim 10, wherein said synthetic oligonucleotide is selected from the group consisting of a phosphorothioate, a phosphorodithioate, a methyl phosphonate and a phosphoramidate.
12. (currently amended): The method of ~~any preceding~~ claim 1, wherein binding of said target oligonucleotide with said titratable anion exchange composition occurs at a pH between 5 and 8.
13. (currently amended): The method of ~~any preceding~~ claim 1, wherein said solution in b) increases in pH in a linear manner over time.
14. (currently amended): The method of ~~any preceding~~ claim 1, wherein said solution in b) increases from a pH of about 8 to a pH of about 11.
15. (currently amended): The method of ~~any preceding~~ claim 1, wherein said solution in b) comprises one or more of NH_4HCO_3 and/or NH_4OH .
16. (currently amended): The method of ~~any preceding~~ claim 1, wherein said target oligonucleotide has a length from about 8 to about 40 nucleotides.
17. (currently amended): The method of ~~any preceding~~ claim 1, wherein said impurity is one or more oligonucleotides having a shorter length than said target oligonucleotide, and wherein said impurity elutes at a lower pH than said target oligonucleotide.
18. (original): The method of claim 17, wherein said impurity is one or more failure sequences.

19. (currently amended): The method of ~~any one of claims 1 to 16~~ claim 1, wherein said impurity is a metal salt.
20. (currently amended): The method of ~~any preceding~~ claim 1, wherein said target oligonucleotide is 5'-O-protected.
21. (currently amended): The method of claim 20, wherein said target oligonucleotide is 5'-O-trityl, ~~preferably 5'-O-dimethoxy-trityl~~, protected.
22. (original): The method of claim 21, further comprising a step of passing through said titratable anion exchange composition a sufficient amount of an acidic solution to cleave said 5'-O-trityl protecting group from said target oligonucleotide prior to eluting said target oligonucleotide.
23. (original): The method of claim 22 wherein said acidic solution comprises aqueous acetic acid.
24. (currently amended): The method of ~~any preceding~~ claim 1, wherein said solution in b) has a volume which is less than the volume of the mixture comprising said target oligonucleotide and impurity, thereby increasing the concentration of said target oligonucleotide.
25. (currently amended): The method of ~~any preceding~~ claim 1, further comprising one or more washing steps prior to eluting said target oligonucleotide.
26. (new): The method of claim 21, wherein said target oligonucleotide is 5'-O-dimethoxy-trityl protected.
27. (new): The method of claim 1, wherein said titratable anion exchange composition comprises polyethyleneimine, polyimidazole, polyhistidine or polylysine conjugated to a synthetic polymer support; said solution in b) is substantially free of metal salts, does not substantially increase its salt concentration over time, increases from a pH of about 8 to a pH of about 11 and comprises one or more of NH_4HCO_3 and/or NH_4OH .